REMARKS

Status of the Claims

Claims 1, 3-6, 8-11, 13-16, and 18-22 are pending in the present application. Claims 2 and 12 are presently canceled, and claims 7 and 17 were previously canceled. Claims 10-11, 13-16, 18-19, and 22 are withdrawn as directed to a non-elected invention. Claim 1, which is presently under examination, and claim 10, which is withdrawn from consideration, are amended without prejudice or disclaimer. Support for these amendments is found in original claims 2 and 12. Claim 9, which is presently under examination, and withdrawn claim 19 are amended for clarity. Specifically, claims 9 and 19 are amended to specify "is sprayed or dripped into the nose" in lieu of "is capable of being sprayed or dripped into the nose." Lastly, claims 5 and 15 are amended to be properly dependent upon claims 3 and 13, respectively. No new matter is added by way of the above amendments. Reconsideration is respectfully requested.

Applicants further point out that no new issues are raised by way of the present submission. For instance, the claims are amended to adopt language from claim 2 or claim 12, which were already searched and considered or to remove issues under 35 U.S.C § 112, second paragraph. Thus, the Examiner is not presented with the burden of additional search and/or consideration.

In the event that the present submission does not place the application into condition for allowance, entry thereof is respectfully requested as placing the application into better form for appeal.

Priority

The Examiner states that Applicants are denied priority to DE 102 35 556.8, filed August 2002, *see* Office Action, page 2. The Examiner further states that an English language translation of the international application is required, when entering the national stage in the United States, *see* Office Action, pages 2. The Examiner, however, does not believe that an English translation of the international application was submitted, *see* Office Action, page 3. In addition, the Examiner states that an English translation of DE 102 35 556.8 was not submitted, *see* Office Action, page 2.

Initially, Applicants note that an English translation of International Application PCT/EP03/08236, of which the instant application is the national stage application, was submitted to the Office on February 1, 2005. The English translation of the International Application is publically available on the Patent Application Retrieval System (PAIR). Specifically, Applicants refer the Examiner to the tagline, which states "Transmittal of New Application." This document states that an English translation of the International Application as-filed is "attached hereto." *See also*, the tags on PAIR dated February 1, 2005, labeled "specification", "claims" and "abstract" for the English translation of the International Application and U.S. Publication No. 2006-0079500, which is based upon the instant application and was published on April 13, 2006.

Applicants further note that an English translation of DE 102 35 556.8 is not required for the instant application to claim the benefit of priority of such document. 37 C.F.R. 1.55 (a)(4) states that (i) An English language translation of a non-English language foreign application is not required except: (A) When the application is involved in an interference; (B) When necessary to overcome the date of a reference relied upon by the examiner, or (C) When specifically required by the examiner. Applicants are not relying on the date of DE 102 35 556.8 to overcome the rejections based upon the art of record. Further, Applicants do not interpret the present comments by the Examiner to indicate that he is requiring Applicants to provide an English translation of DE 102 35 556.8. Accordingly, Applicants believe that they have properly requested priority under 35 U.S.C. § 119(a).

Issue Under 35 U.S.C. § 112, second paragraph

Claim 9 is rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Specifically the Examiner states that the phrase "is capable of being" sprayed or dripped into the nose is unclear. Although Applicants do not agree that the claim lacks clarity, claim 9 is amended to expedite prosecution. As amended, the phrase "is capable of being" has been replaced with the unambiguous "is." Accordingly, the claim is not unclear and Applicants respectfully request withdrawal of the rejection.

Issues Under 35 U.S.C. § 103(a)

Claims 1-6, 8, 9, 20, and 21 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Publication No. 2002/0019421 to Biberman, ("Biberman"), in view of U.S. Publication No. 2003/0060423 to Plata-Salaman, ("Plata-Salaman"), *see* Office Action, pages 5-11. Applicants respectfully traverse.

The Examiner states that the claims are generally directed to a composition consisting of two administration forms: 1) an administration form that continuously releases at least one modulator of nicotinic receptors and 2) an administration form which enables a rapid entry of galanthamine, *see* Office Action, page 6. The Examiner alleges that Biberman describes a pharmaceutical composition comprising a monoamine oxidase inhibitor, an addictive substance, such as nicotine, and a suitable carrier, *see* Office Action, page 7. In addition, the Examiner states that Biberman teaches that the above-described combination may further comprise an inhibitor of acetylcholine esterase or a nicotine antagonist such as galanthamine hydrobromide, *see* Office Action, page 7. The Examiner further states that Biberman teaches that nicotine and an MAO inhibitor may be co-administered *via* different routes, *e.g.*, buccal, and in a variety of forms such as in aerosol form, *see* Office Action, page 8.

The Examiner admits that Biberman does not expressly describe the rapid release form containing 1-5 mg of galanthamine as specified in claim 6, *see* Office Action, page 8. The Examiner further admits that Biberman does not expressly teach that the modulator of the nicotinic receptors is solely galanthamine, *see* Office Action, page 8.

The Examiner alleges, however, that Plata-Salaman describes co-therapy compositions, *i.e.*, at least one compound of a general "formula I", which is administered with at least one acetylcholinesterase inhibitor, *e.g.*, galanthamine, *see* Office Action, page 8. In addition, the Examiner states that Plata-Salaman teaches that the compounds in the co-therapy composition are administered simultaneously, sequentially, separately, or in a single pharmaceutical formulation, *see* Office Action, page 8. The Examiner also asserts that Plata-Salaman teaches that, where dosing does not occur in a single formulation, the routes of administration may be varied, *e.g.*, intranasal, and further include immediate release dosage forms, timed dosage forms and sustained release dosage forms, *see* Office Action, page 8.

Based upon the foregoing, the Examiner contends that it would have been obvious to a person of ordinary skill in the art to prepare a medicament consisting of two independent, but concurrently administered, dosage forms, wherein one or both forms comprise galanthamine, as taught by Biberman, and wherein the dosage forms have different rates of delivery, as inherently described by the combination of Biberman and Plata-Salaman, to achieve the instant invention, *see* Office Action, page 9. Accordingly, the Examiner believes that it would have been *prima facie* obvious to combine the cited references, each of which allegedly is useful for treating addictions, to achieve the instantly claimed invention, *see* Office Action, page 10. Applicants respectfully disagree.

The Examiner Has Failed to Present a *Prima Facie* Case of Obviousness

The burden is on the Examiner to make a *prima facie* case of obviousness, which requires an objective analysis as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). In *KSR International v. Teleflex Inc.*, 82 USPQ2d 1385 (2007), the Court affirmed that this analysis includes the following factual inquires: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the claimed invention and the prior art; and (3) resolving the level of ordinary skill in the pertinent art. The Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in view of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* state that, having undertaken the factual inquires of *Graham*, a rejection under 35 U.S.C. § 103 may be supported by one or more of the following rationales: (1) combining prior art elements according to known methods to yield predictable results; (2) simple substitution of one known element for another to obtain predictable results; (3) use of a known technique to improve similar devices in the same way; (4) applying a known technique to a known device ready for improvement to yield predictable results; choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (5) variations that would have been predictable to one of ordinary skill the art; and (6) some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine the prior art reference teachings to arrive at the claimed invention. 72 Fed. Reg. 57526, at 57529 (October 10, 2007). Each of the above-noted rationales requires

predictability in the art and/or a reasonable expectation of success, and the Examiner must consider objective evidence, which rebuts such predictability and reasonable expectation of success. This objective evidence or secondary considerations may include unexpected results and/or failure of others (*e.g.*, evidence teaching away from the currently claimed invention), evidence of commercial success, and long-felt but unsolved needs, as found in the specification as-filed or other source. *Id.* When considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." 82 USPQ2d at 1389.

The Present Invention

Independent claim 1 is directed to a medicament for treating addiction craving, characterized in that the medicament consists of a combination of two administration forms, one of the administration forms continuously releasing at least one modulator of nicotinic receptors, which is selected from the group consisting of galanthamine and the pharmacologically acceptable salts of galanthamine, and the other administration form enabling a rapid entry of galanthamine or one of its pharmacologically acceptable salts into the central nervous system, wherein the administration form, which enables a quick entry of galanthamine, or a pharmacologically acceptable salt of galanthamine, into the central nervous system, is selected from the group consisting of: buccal solutions, spray solutions and drip solutions.

The Cited Art Fails to Render the Present Invention Obvious

Biberman teaches a pharmaceutical composition comprising an inhibitor of monoamine oxidase ("MAOI"), an amount of an addictive substance, or a derivative thereof, wherein said substances are applied on a suitable carrier for the treatment of addictions and addiction cravings, *see. e.g.*, abstract, claim 1 and paragraph [0104] of Biberman. In addition, Biberman teaches that an acetylcholinesterase inhibitor is, optionally, included in the composition. Biberman further teaches that the MAOI and the addictive substance are always applied simultaneously and are only effective in combination, *see., e.g.*, Experiment 1 and paragraph [0135] of Biberman. Biberman also teaches that acetylcholinesterase inhibitors only enhance the

effect of the MAOI and addictive substance combination, *see, e.g.*, paragraphs [0069] and [0071].

Plata-Salaman describes the co-administration of an anticholinergic drug and an anticonvulsant for the treatment of dementia or memory disorders, *see* abstract. The dementia may result from, *e.g.*, Alzheimer's, brain damage or alcoholism, *see, e.g.*, claim 10 of Plata-Salaman.

The references do not teach or suggest the claimed elements

Applicants submit that the cited references do not teach or suggest the instantly claimed medicament. The medicament, as claimed, *consists* of a combination of two administrative forms, one form continuously releasing at least one modulator of nicotinic receptors, which is selected from the group consisting of galanthamine and the pharmacologically acceptable salts of galanthamine, and the other administrative form, which enables a quick entry of galanthamine or a pharmacologically acceptable salt of galanthamine into the central nervous system, *i.e.*, buccal solutions, spray and drip solutions. In contrast, Biberman teaches that the MAOI and the addictive substance are to be applied simultaneously and are only effective in combination, *see., e.g.*, Experiment 1 and paragraph [0135] of Biberman. Biberman further teaches that the active substance, MAOI, is essential in the treatment of dependencies, while acetylcholinesterase inhibitors, *e.g.*, galanthamine, only enhance the effect of the MAOI/addictive substance combination, *see e.g.*, paragraphs [0069] and [0071]. Accordingly, an ordinary artisan would not have been able to predict that glanthamine, alone, *i.e.*, without MAOI's and/or addictive substances, would have been useful when administered in two different forms to reduce addiction cravings.

Plato-Salamon does not remedy the deficiencies of Biberman. Plato-Salaman describes a dementia therapy, not a therapy for addictive cravings, which comprises an anticonvulsant in combination with an acetylcholinesterase inhibitor, *e.g.*, galanthamine. Accordingly, none of the cited references, either alone or in combination, teach or suggest the claimed medicaments, which do not rely on MAOIs, and/or addictive substances, and/or anticonvulsants, to treat addiction cravings.

An ordinary artisan is not motivated to combine the references

Applicants further submit that an ordinary artisan would have not been motivated to combine the cited references. As noted above, Biberman describes a medicament for treating an addiction and addiction cravings. Plato-Salaman does not pertain to the treatment of addiction cravings, *e.g.*, alcohol cravings and/or nicotine cravings, *see* claim 10 of Plato-Salaman, and *see also* response filed June 18, 2008. Instead, Plato-Salaman is directed to the treatment of dementia or memory disorders. Such disparate disorders, *i.e.*, addiction cravings and dementia, are based upon entirely different physiological defects and are treated with entirely different medicament combinations, *i.e.*, an MAOI and an addictive substance (Biberman) or an anticholinergic drug and an anticonvulsant (Plato-Salaman). Accordingly, an ordinary artisan would have not have been motivated to combine references that are directed to the treatment of different diseases to achieve an improved pharmacological withdrawal therapy as described in the instant claims.

Unexpected Results

In addition, Applicants submit that the claimed medicaments have advantages that would not have been expected from the cited references by an ordinary artisan. The claimed medicaments are useful as an improved pharmacological withdrawal therapy, which effectively combats the break-through cravings for alcohol and/or nicotine that can occur, despite an ongoing basal level of pharmacological withdrawal therapy. As noted in Exhibit A, the claimed medicament results in a synergistic reduction in alcohol use, *i.e.*, a 40% reduction, and a synergistic reduction in cigarette use, *i.e.*, a 34% reduction in comparison to an ongoing basal level of galanthamine treatment only, which reduced alcohol and cigarette consumption by only a moderate amount, *see* Exhibit A, enclosed. This reduction in alcohol and cigarette use, which is attributed to mitigating break-through cravings, could not have been predicted from the cited references since neither of the documents addresses the problem of treating such cravings.

Further, the instantly claimed medicaments can reduce addiction cravings without the addition of addictive substances, which results in significant advantages and is unexpected in view of the cited references. For example, Biberman teaches that addiction cravings, *e.g.*, nicotine or alcohol cravings, are reduced by providing a medicament, which comprises the

addictive substance. That is, if a subject is suffering from, *e.g.*, alcoholism, Biberman teaches and/or suggests a medicament comprising alcohol to reduce such cravings. However, the advantage of reducing cravings by providing an addictive substance in a medicament also results in serious disadvantages since even low concentrations of addictive substances have a dependency potential, *see* page 5, paragraph 1 of the originally filed application. Accordingly, Biberman's treatment method is contraindicated in a patient suffering from addictions, such as alcoholism. In contrast, the presently claimed medicaments, surprisingly, result in decreased cravings without resorting to addictive substances, which are contraindicated in addictive disease, *e.g.*, alcoholism, and can potentially can cause new, and, accordingly, counterproductive dependencies, or worsen dependencies. Further, the claimed medicaments may be used for treating a wide variety of addictions without concomitantly subjecting the patient to the addictive substance in the medicament.

The instantly claimed medicaments provide further unexpected advantages, *i.e.*, the medicaments allow for a continuous administration of active substances, at a concentration that can be minimized to mitigate side effects, while treating break-through cravings only as required. Biberman's disclosure would not have suggested such advantages to an ordinary artisan. As noted above, Biberman teaches that the active substance, MAOI, is essential in the treatment of dependencies, while acetylcholinesterase inhibitors, *e.g.*, galanthamine, only enhance the effect of the MAOI/addictive substance combination. Accordingly, an ordinary artisan would not have been able to predict from the cited references that glanthamine, alone, could have been provided in two administration forms, wherein one application form provides a steady concentration of the active substance resulting in decreased cravings and the second application form provides a rapid onset of active substance, resulting in a reduction in break-through cravings, as needed.

Based upon the foregoing, Applicants submit that the claims are not obvious over cited references. Accordingly, Applicants respectfully request withdrawal of the rejection.

In view of the fact that the elected product of claim 1 is allowable, the Examiner is requested to rejoin the non-elected method claims, which include all limitations of the allowable products. Rejoinder is proper pursuant to MPEP § 821.04.

CONCLUSION

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: APR 10 2009

Respectfully submitted,

By _____

Craig A. McRobbie
Registration No.: 42,874
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant